



LETTER TO CHIEF DRAFTSMAN

Date: March 12, 2008

**Fig. 1a****Stage I**

Undifferentiated embryonic stem cells
cultured on feeder cells



nestin

Stage II (7 days)

Generation of ~~nestin~~ ^{nestin} positive islet cell progenitors in
suspended embryoid bodies

**Stage III (7 days)**

Culture of embryoid bodies in ITSF medium:
elimination of nestin negative cells/progenitor isolation

**Stage IV (7 days)**

Culture of progenitors with N2, B27, bFGF
supplementation: expansion of progenitors

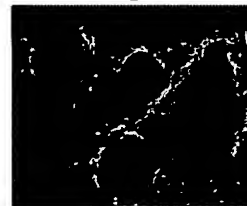
**Stage V (14 days)**

Replacement of bFGF with nicotinamide and reduction of
glucose concentration to 5 mM: generation of surface-bound
islet like clusters containing insulin producing cells

**Stage VI (14 days)**

Suspension culture of dissociated surface-bound clusters:

- generation of purified suspended islet like clusters
- steep increase in insulin secretion capacity
- purification of insulin producing cells
- prolongation of *in-vitro* longevity of insulin producing cells

Fig. 1b**Fig. 1c****Fig. 1d****Fig. 1e****Fig. 1f****Fig. 1g**